Benedetto, U., Caputo, M., Angelini, G., Bryan, A., Gaudino, M., & Mariscalco, G. (2016). Impact of multiple arterial grafts in off-pump and on-pump coronary artery bypass surgery. *Journal of Thoracic and Cardiovascular Surgery*, *153*(2), 300-309. https://doi.org/10.1016/j.jtcvs.2016.10.084

Impact of multiple arterial grafts in off-pump and on-pump coronary artery bypass surgery.

Umberto Benedetto[1] PhD, Massimo Caputo[1] MD, Giovanni Mariscalco[2] PhD, Mario Gaudino[3] MD, Pierpaolo Chivasso MD[1], Alan Bryan[1] MD, Gianni D Angelini[1] MD.

[1]Bristol Heart Institute, University of Bristol, School of Clinical Sciences, Bristol, United Kingdom.

[2]Glenfield General Hospital, University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom.

[3]Department of Cardiothoracic Surgery, Weill Cornell Medical College, New York, NY

Word count: 3270

No potential conflicts exist for all authors

Acknowledgement: This study was supported by the British Heart Foundation and the NIHR Bristol Cardiovascular Biomedical Research Unit.

Corresponding Author

Umberto Benedetto MD PhD

Bristol Heart Institute, University of Bristol

Upper Maudlin St, Bristol BS2 8HW

Tel: +44 (0) 117 923 0000

Email: umberto.benedetto@bristol.ac.uk

Abbreviations

ASMD: absolute standardized mean difference

BITA: bilateral internal thoracic artery

BMI: body mass index

CCS: Scandinavian cardiovascular Society

COPD: chronic obstructive pulmonary disease

CVA: cerebrovascular accident

DM: diabetes mellitus

EES: effective sample size

IABP: intra-aortic balloon pump

MA: multiple arteries

MI: myocardial infarction

NYHA: New York Heart Association

ONCAB: on-pump coronary artery bypass

OPCAB: off-pump coronary artery bypass

PCI: percutaneous coronary intervention

PVD: peripheral vascular disease

RA: radial artery

RRT: renal replacement therapy

SA: single Artery

SVG: saphenous vein graft

Central message

Multi-arterial grafting is associated with improved late survival following on- and off-pump CABG. Off-pump surgery is associated with similar survival as on-pump surgery, when controlling for the extent of arterial revascularization.

Perspective statement

There is growing concern that off-pump coronary artery bypass is associated with reduced long-term survival compared with traditional on-pump surgery. However, most available comparisons focus on single artery revascularization. We found that off-pump multiple arterial grafting is superior to standard on pump single arterial revascularization. Therefore, multiple arterial grafting should be the standard strategy in randomized studies comparing off-pump with on-pump surgery.

Abstract:

Objective(s): There is growing concern that off-pump coronary artery bypass (OPCAB) is associated with reduced long-term survival compared with traditional on-pump coronary artery bypass (ONCAB). However most of available comparisons between OPCAB and ONCAB focus on single artery (SA) revascularization. We sought to investigate the impact of using multiple arterial (MA) conduits in the comparison between OPCAB versus ONCAB by performing a single centre long term propensity score base analysis.

Methods: The study population included 5195 SA-ONCAB, 1208 MA-ONCAB, 4412 SA-OPCAB and 1818 MA-OPCAB procedures. Late survival was available for all cases (100%). Inverse Propensity score weighting and time segmented Cox model were used for multiple treatments comparison.

Results: No significant differences were found between the four groups in terms of 30-day mortality, postoperative cerebrovascular accident and renal replacement therapy between the four groups. After a mean follow-up time of 8.2±4.7 years, in the PS-weighted sample, survival probabilities at 10 years were 74.5±0.4, 79.7±0.4, 73.4±0.5 and 79.0±0.5 in the SA-ONCAB, MA-ONCAB, SA-OPCAB and MA-OPCAB groups respectively. Propensity-weighted analysis confirmed that MA-OPCAB (HR 0.81;95%CI 0.69-0.98) and MA-ONCAB (HR 0.81;95%CI 0.65-0.99) were associated with a lower late mortality when compared to standard SA-ONCAB.

Conclusions: OPCAB with multiple arterial grafts is as safe as the conventional ONCAB and achieves excellent long term survival rates which are superior to those observed after standard SA-ONCAB and comparable to MA-ONCAB.

Keywords: off-pump coronary artery bypass grafting; multiple arterial grafting; survival; propensity score

There is growing concern that off-pump coronary artery bypass (OPCAB) is associated with reduced long-term graft patency of saphenous vein grafts (SVGs) [1-4] and this might translate into inferior long-term survival compared with traditional on-pump coronary artery bypass (ONCAB) [5]. On the other hand, OPCAB has been associated with arterial graft patency rates comparable to those after ONCAB [4]. Technical issues and the learning curve, the inflammatory and prothrombotic state in OPCAB patients have been suggested as an explanation for the reported inferior graft patency rate. There is also evidence that patients operated on-pump have significantly higher saphenous graft mean flow in comparison with patients operated off-pump with no difference in these parameters for arterial grafts [6]. As a consequence, the use of multiple arterial (MA) grafts including the bilateral internal thoracic arteries (BITA) [7,8] and the radial artery (RA) instead of SVGs [7,9] in OPCAB has recently gained popularity [10-12]. However most of available comparisons between OPCAB and ONCAB focus on single artery (SA) revascularization [13-18]. We sought to investigate the impact of using multiple arterial conduits in the comparison between OPCAB versus ONCAB by performing a single centre long term propensity score base comparison. We also investigated the effects of incomplete revascularization following each of the treatment strategies.

Methods

The study was conducted in accordance with the principles of the Declaration of Helsinki. The local audit committee approved the study, and the requirement for individual patient consent was waived. We retrospectively analysed prospectively collected data from The National Institute for Cardiovascular Outcomes Research (NICOR) NACSA registry on 1 June 2015 for all isolated first time CABG procedures performed at the Bristol Heart Institute, Bristol United Kingdom from 1996 to April 2015. Reproducible cleaning algorithms were applied to the database, which are regularly updated as required. Briefly, duplicate records and non-adult

cardiac surgery entries were removed; transcriptional discrepancies harmonized; and clinical conflicts and extreme values corrected or removed. The data are returned regularly to the local units for validation.

Further details and definition of variables are available at http://www.ucl.ac.uk/nicor/audits/adultcardiac/datasets. Among 15119 isolated first time CABG cases performed at our institution during the study period**,** we selected subjects who met the following criteria: first time isolated CABG; multivessel coronary disease and/or left main disease; requiring at least 2 grafts; CABG performed by using the following four strategies: on pump single left internal thoracic artery grafting (LITA) plus additional SVGs (SA-ONCAB, reference group); on pump multiple arterial grafting (by using LITA plus RITA and/or RA) with or without additional SVGs (MA-ONCAB); off pump single internal thoracic artery grafting plus additional SVGs (SA-OPCAB); off pump multiple arterial grafting (by using LITA plus RITA and/or RA) with or without additional SVGs (MA-OPCAB, video 1). In the present series, the surgical strategy was based on individual surgeon preference and expertise. In the present series, the RA was considered only in case of target stenosis ≥75% and it was used a free graft proximally connected to the ascending aorta. The internal thoracic artery was used as a pedicle graft that remained proximally connected to its respective subclavian artery (in situ) or as a free graft proximally connected to other internal thoracic artery.

Pre-treatment variables and study end-points

The effect of MA conduits and OPCAB was adjusted for the following pre-treatment variables including: age, gender, body mass index (BMI); Canadian Cardiovascular Society (CCS) grade III or IV; New York Heart Association grade III or IV; previous myocardial infarction (MI) and MI within 30 days, previous percutaneous coronary intervention (PCI); diabetes mellitus (DM) on oral treatment or on insulin (DM-I); chronic obstructive pulmonary disease (COPD);

current smoking; serum creatinine ≥200 mmol/l, previous cerebrovascular accident (CVA); peripheral vascular disease (PVD); preoperative atrial fibrillation (AF); left main disease (LMD); 3-vessel disease (TVD); left ventricular ejection fraction (LVEF) between 30% and 49%; LVEF less than 30%; non elective admissiom, emergent/salvage operation; cardiogenic shock; preoperative intra-aortic balloon pump (IABP) and year of surgery. Logistic EuroSCORE was used as measure of overall risk profile but not included in the propensity score model.

The short-term outcomes investigated were: the incidence of re-exploration for bleeding, need for sternal wound reconstruction, postoperative CVA (defined as any confirmed neurologic deficit of abrupt onset that did not resolve within 24 hours), postoperative renal replacement therapy (RRT), need for postoperative IABP and early mortality (within 30 days). We also reported as short term outcomes, incomplete revascularization (IR), defined as at least one diseased primary arterial territory not grafted. Long-term outcome investigated was all-cause late mortality. Information about post-discharge mortality tracking was available for all patients (100%) and was obtained by linking the institutional database with the National General Register Office.

Statistical analysis

For baseline characteristics, variables are summarised as mean for continuous variables and percentage for categorical variables. The chi squared test was used to test unadjusted association between treatment variable and outcomes. Multiple imputation (m=3) was used to address missing data (165 patients). Rubin's method [19] was used to combine results from each of *m* imputed data sets.

Inverse probability (propensity score) of treatment weighting (IPSW) for modelling causal effects was used for multiple treatments comparison [20]. A generalised boosted model was implemented to estimate multinomial propensity scores (PS) adjusting for pre-treatment

covariates, and the propensity score was assumed as the probability that an individual with pre-treatment characteristics X receives treatment t (twang R package).The average treatment effect on the population (ATE) was used to answer the question of how, on average, the outcome of interest would change if everyone in the population of interest had been assigned to a particular treatment relative to if they had all received another single treatment. To estimate the ATE, we gave treated patients weight $w_i = 1/(1 – p(x_i))$, where p(xi) is the propensity score, and reference patients $w_i = 1/p(x_i)$. SA-ONCAB was considered as the reference group in all comparisons. The absolute standardised mean difference (ASMD) was used as a balance metric to summarize the difference between two univariate distributions of a single pre-treatment variable. A value ≥0.20 was considered as an indicator of imbalance [21]. Although all subjects are retained using IPSW, weighted means can have greater sampling variance than unweighted means from a sample of equal size. To account for such observation, we calculated the effective sample size (ESS) which gives an estimate of the number of comparison participants that are comparable to the treatment group [20]. We then estimated the treatment effect estimates by using weighted logistic regression models for postoperative complications and weighted time-segmented Cox models for early (within 30 days) and late (beyond 30 days) mortality. These models contained only a treatment indicator. Lastly, we estimated the treatment effect within subgroups according to the presence of incomplete revascularization, total arterial revascularization and era of surgery. R version 3.1.2 (2014-10-31) was used for all statistical.

Results

Study population

The study population included 5195 SA-ONCABs, 1208 MA-ONCABs, 4412 SA-OPCAB and 1818 MA-OPCABs (Figure 1). Preoperative variables distribution in the four groups is summarized in Table 1. In the unweighted population, SA-ONCAB and SA-OPCAB groups tended to present a higher burden of comorbidities when compared to MA-ONCAB and MA-

OPCAB. In particular SA-ONCAB and SA-OPCAB patients were more likely to older, female, and present NYHA III-IV functional class, COPD and LVEF≤30%. SA-ONCAB cases were more likely to have 3-vessel disease when compared to the other groups (Supplementary Table 1). After PS-weighting the four groups were comparable for all pre-treatment variables (ASMD<0.20, Table 2, Supplementary Table 2, Supplementary Figure 1). Although the original MA-ONCAB and MA-OPCAB groups had 1208 and 1818 cases respectively, the propensity score estimates effectively utilized only 388 and 739 of the comparison cases with a significant loss of sample size. This indicates that many of the original cases were not useful for isolating the treatment effect.

Intraoperative data

Intraoperative data are summarized in Table 3. Among patients receiving MA conduits, BITA was used more often during ONCAB whilst RA was used more often during OPCAB. However the overall rate of total arterial revascularization was comparable between ONCAB and OPCAB. Overall, numbers of grafts were lower among OPCAB cases. Both circumflex artery and right coronary artery territories were less likely to be grafted during OPCAB, but this was more evident among SA-OPCAB cases. The overall incidence of IR was higher among OPCAB in particular after SA-OPCAB. However, the majority of MA-OPCAB cases received complete revascularization (91.3%) and the absolute increase in IR rate in the MA-OPCAB group was marginal when compared to SA-ONCAB (+2.9%) and MA-ONCAB (+3.5%).

Short term outcomes

Observed 30-days mortality and rate of postoperative complications are summarized in Table 4. Unadjusted treatment effect estimates on outcomes of interest are summarized in Table 5. Overall crude 30-day mortality rate was 152(1.2%) with a significant trend towards a reduced mortality with MA-ONCAB and MA-OPCAB when compared to standard SA-ONCAB. The

crude incidences of postoperative CVA, IABP and RRT were significantly lower in MA-OPCAB. SA-OPCAB and MA-OPCAB were associated with a reduced rate of re-exploration for bleeding. However, this observed trend towards a reduced morbidity and early mortality in the MA-OPCAB group was correlated to the higher burden of comorbidities observed in SA-ONCAB and SA-OPCAB groups rather than a real treatment effect. In fact, after PS-weighting (Table 5), no significant differences were found between the four groups in terms of 30-day mortality, postoperative CVA and RRT between the four groups. However, OPCAB still remained associated with a trend towards reduced incidence of postoperative IABP and re-exploration for bleeding. In the PS-weighted analysis OPCAB remained associated with a 2-fold increased risk of incomplete revascularization regardless of the use of multiple arterial grafts.

Long term survival

After a mean follow-up time of 8.2±4.7 years, there were 1583(30%), 195(16%), 1103(25%) and 269(15%) deaths in the SA-ONCAB, MA-ONCAB, SA-OPCAB and MA-OPCAB groups respectively. In the unweighted sample, survival probabilities at 10 were 72.4±0.7, 89.3±0.9, 69.7±0.9 and 83.7±0.1 and in the SA-ONCAB, MA-ONCAB, SA-OPCAB and MA-OPCAB groups respectively. In the PS-weighted sample, survival probabilities at 10 years were 74.5±0.4, 79.7±0.4, 73.4±0.5 and 79.0±0.5 in the SA-ONCAB, MA-ONCAB, SA-OPCAB and MA-OPCAB groups respectively (Figure 2 left). In the unweighted sample SA-OPCAB was associated with a lower survival when compared to the standard SA-ONCAB whilst MA-ONCAB and MA-OPCAB were associated with better late survival (Table 4). PS-weighted analysis (Figure 2 right) confirmed that MA-OPCAB and MA-ONCAB were associated with a relative 20% risk reduction in late mortality when compared to standard SA-ONCAB whilst PS-weighted SA-OPCAB did not significantly increase the risk of late death (Table 4). When the analysis was restricted to subjects who had complete revascularization, MA-OPCAB (adj

HR 0.80;95%CI 0.65-0.97; P=0.02) and MA-ONCAB (adj HR 0.80;95%CI0.63-0.99; P=0.04) but not SA-OPCAB (adj HR 1.05; 95%CI 0.94 1.17; P=0.39) were associated with a reduced risk of late death when compared to SA-ONCAB. On the other hand, among subject with incomplete revascularization, we found that neither MA-OPCAB (adj HR 0.95;95%CI 0.62-1.46; P=0.82) or MA-ONCAB (adj HR 1.06; 0.60-1.90; P=0.83) or SA-OPCAB (adj HR 1.07;95%CI 0.77-1.48; P=0.69) were associated with better long term survival when compared to SA-ONCAB (Supplementary Figure 2). **We could not demonstrate a superiority in terms of late survival by using total arterial OPCAB (adj HR 0.77; 95%CI 0.60-0.98) instead of MA-OPCAB with additional SVGs (adj HR 0.71;9%%CI 0.57-0.89) or by using total arterial ONCAB (adj HR 0.84; 95%CI 0.64-1.09) instead of MA-ONCAB with additional SVGs (adj HR 0.57;95%CI 0.42-0.78) over the standard SA-ONCAB strategy (Supplementary Figure 3)**. However the incidence of IR among total arterial-OPCAB and total arterial-ONCAB was particularly high (20% and 12% respectively) when compared to MA-OPCAB with additional SVGs (0%) and MA-ONCAB with additional SVGs (0.4%) and this aspect might have caused an underestimation of the effect of total arterial revascularization. The effect of era of surgery was also investigated **(Supplementary Figure 4)**. When compared to SA-ONCAB, MA-OPCAB was associated with reduced late mortality during the era 1996-2004 (adj HR 0.83; 95%CI 0.64-0.99) and 2005-2009 (adj HR 0.73;95%CI 0.55-0.96) while the two strategies were comparable after 2010 and this is partially explained by the relatively short follow-up duration (<5 years). When compared to standard SA-ONCAB, MA-OPCAB also did not increase early mortality across eras (1996-2004: HR 0.88;95%CI 0.25- 3.01; after 2010 MA-OPCAB: HR 0.28; 95%CI 0.03 -2.15 respectively).

Discussion

The main finding of the present study is that MA-OPCAB can be performed with a very low operative mortality and morbidity. Complete revascularization with MA-OPCAB was achieved in the majority of patients (92.3%). MA-OPCAB with complete revascularization was associated with excellent long term survival rates which are at least comparable to those observed after MA-ONCAB and significantly superior to those observed after SA-ONCAB. SA-OPCAB was associated with poorer long term survival when compared to SA-ONCAB although this difference was no longer statistically significant after risk adjustment. Among cases with incomplete revascularization we could not identify any difference between ONCAB and OPCAB in terms of late survival regardless the use of MA grafts although this analysis was largely underpowered. In the present analysis we used all-cause mortality to assess treatment effect on long term. All cause-mortality is considered the most robust and unbiased index in cardiovascular research because no adjudication is required, thus avoiding inaccurate or biased documentation and clinical assessments [22]. The four groups were compared using inverse propensity score weighting. One of the advantages of this technique over standard pairwise propensity matching is the possibility of simultaneous comparisons between multiple treatments. Moreover, all the individuals in the study can be used for the outcomes evaluation whilst a large number of subjects may not be used in a propensity matching.

Whether OPCAB surgery is superior to traditional ONCAB surgery remains one of the most controversial areas of cardiac surgery. In North America, OPCAB procedures peaked at 25% in 2004 and have declined steadily since that time [23]. Among possible explanations, there is growing concern that OPCAB is associated with reduced long-term graft patency thus resulting in inferior long-term survival compared with traditional ONCAB as observed by some authors [5]. However, meta-analyses of currently available randomized controlled trials on graft patency have shown that OPCAB increases the incidence of SVG graft occlusion only but does not affect internal thoracic artery and RA graft patency when compared with ONCAB [4]. As

a consequence recent reports advocate for a more extensive use of arterial grafts during OPCAB in order to improve OPCAB results. Suzuki et al. [10] recently reported on 260 cases undergoing OPCAB with SVG and 520 cases of OPCAB with total arterial revascularization and total arterial OPCAB was protective in terms of late cardiac events (HR 0.5;95%CI 0.31–0.84; P=0.007). In a previous study, Kinoshita et al. [11] compared off-pump skeletonized single (n=236) versus bilateral (n=300) internal thoracic artery grafting in high risk cases (Euroscore≥5). After a mean follow-up of 3.2 years, BITA grafting was significantly associated with a lower risk of overall death (hazard ratio, 0.56; 95% CI, 0.32 to 0.87; P=0.009). Navia et al. recently compared 1447 OPCAB cases with BITA grafting versus and 253 OPCAB with received left internal thoracic artery and radial artery grafting [12]. They found that the two strategies where comparable in terms of late mortality (P=0.65) although BITA grafting was associated with lower postoperative reintervention/readmission-free survival (P=0.03).

However, available randomized comparative studies on long term survival after OPCAB versus ONCAB included mainly procedure with left internal thoracic artery to left anterior descending artery and small number of other arterial grafts [13-18]. Therefore, the impact of multiple arterial grafts on long term survival after OPCAB versus ONCAB still needs to be determined. To date few studies focused on early outcomes after MA-OPCAB versus MA-ONCAB. Kobayashi et al. [24] reported on 167 consecutive unselected patients randomly assigned to undergo MA-OPCAB (n=81) or MA-ONCAB (n=86) and they found that the incidence of perioperative complications was similar. In the BITA arm of the Arterial revascularization trial (ART) [25], OPCAB and ONCAB were found comparable in terms of 1 year outcomes.

The completeness of revascularization has been a major concern in OPCAB. As OPCAB with arterial grafts is thought to be technically demanding, incomplete revascularization might limit its benefit on long term survival [26]. In a recently published large series, [25] Omer et al reported a 29% rate of IR in 6367 OPCAB cases compared to 11.0% in 34,772 ONCAB cases.

However, in the present series, IR rate in the MA-OPCAB group was relatively low and only marginally higher than MA-ONCAB (8.7% versus 5.2%). These findings confirmed that complete revascularization can be achieved in MA-OPCAB in the majority of cases and this conclusion is supported by previous reports. In their randomized trial, Kobayashi et al. [24] found that completeness of revascularization (completed grafts/planned grafts) was 98% in both MA-OPCAB and MA-ONCAB groups. In the BITA arm of the ART [24], OPCAB and ONCAB groups showed comparable number of grafts per patient. Of note, in a recent report on the Veterans Affairs Continuous Improvement in Cardiac Surgery Program [26] involving 41,139 patients with left main and 3-vessel coronary artery disease, the IR rate among 6367 OPCAB cases was remarkably high (29%) compared to that observed in 34,772 ONCAB cases (11.0%). A possible explanation for the relatively low IR rate observed in our MA-OPCAB series is the high OPCAB volume at our centre performed by experienced surgeons during the study period. The high OPCAB volume can also partially account for the quasi-equipoise between OPCAB and ONCAB in patients receiving a single arterial graft, thus confirming a central role of surgeon experience in determining outcomes after myocardial revascularization without cardiopulmonary bypass [27].

Limitations

Although the data were collected prospectively, the main limitation is the retrospective analysis. It is possible that patients receiving MA conduits where younger and healthier. Propensity technique can adjust only for measurable and included variables and we cannot exclude a selection bias based on non-measurable "eye-ball". Moreover, we were unable to provide specific causes of death (cardiac vs non-cardiac) as well as incidence of major cardiac adverse events including myocardial infarction and repeat revascularization and therefore, we can only speculate that the mechanism beyond the equipoise between OPCAB and ONCAB on long-term survival. Another limitation of this study is that OPCAB was performed by

experienced surgeons and the results may not be the same with surgeons in their learning curve period or in low volume OPCAB centres. These results might be true only for cardiac surgeons and anaesthesiologists who are fully accustomed to OPCAB. Furthermore, patients might have been selected for MA grafting OPCAB only when complete revascularization was deemed possible. The use of MA grafts has declined in t recent years. In our healthcare system there is an increasing demand for reducing resource utilization and this might influence surgeons in adopting MA grafting which is more time consuming. It can also be speculated that the use of the radial artery was often preferred over a second internal thoracic artery as anticipated to be less time consuming and technically demanding. The decrease in the number of OPCAB procedures in recent years in our centre, can be explained with the appointment of two young surgeons with no previous training in this technique, the retirement of one of the most senior OPCAB surgeon and the part time position of the senior surgeon who first introduced the technique.

In conclusion, multi-arterial grafting was associated with improved late survival following on- and off-pump CABG. Off-pump was consistently associated with a lower risk of need for IABP postoperatively and re-exploration and it was associated with similar 10 years survival as on-pump surgery, when controlling for the extent of arterial revascularization. Complete revascularization during OPCAB is achievable in the majority of cases and it should still be the main goal while performing OPCAB surgery in order to optimize outcomes after surgical revascularization.

References

1. Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, et al; Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group.On-pump versus off-pump coronary-artery bypass surgery. N Engl J Med. 2009;361:1827-37.

2. Houlind K, Fenger-Grøn M, Holme SJ, Kjeldsen BJ, Madsen SN, Rasmussen et al.; DOORS Study Group. Graft patency after off-pump coronary artery bypass surgery is inferior even with identical heparinization protocols: results from the Danish On-pump Versus Off-pump Randomization Study (DOORS).J Thorac Cardiovasc Surg. 2014;148:1812-1819.
3. Takagi H, Matsui M, Umemoto T. Lower graft patency after off-pump than on-pump coronary artery bypass grafting: an updated meta-analysis of randomized trials. J Thorac Cardiovasc Surg. 2010;140:e45-7.
4. Zhang B, Zhou J, Li H, Liu Z, Chen A, Zhao Q. Comparison of graft patency between off-pump and on-pump coronary artery bypass grafting: an updated meta-analysis. Ann Thorac Surg. 2014;97:1335-41.
5. Kim JB, Yun SC, Lim JW, Hwang SK, Jung SH, Song H, Chung CH, Lee JW, Choo SJ. Long-term survival following coronary artery bypass grafting: off-pump versus on-pump strategies. J Am Coll Cardiol. 2014;63:2280-8.
6. Paparella D, Galeone A, Venneri MT, Coviello M, Scrascia G, Marraudino N et al. Activation of the coagulation system during coronary artery bypass grafting: comparison between on-pump and off-pump techniques. J Thorac Cardiovasc Surg 2006;131:290-297
7. Benedetto U, Raja SG, Albanese A, Amrani M, Biondi-Zoccai G, Frati G. Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trials. Eur J Cardiothorac Surg. 2015;47:59-65.
8. Benedetto U, Amrani M, Gaer J, Bahrami T, de Robertis F, Simon AR, Raja SG; Harefield Cardiac Outcomes Research Group.The influence of bilateral internal mammary arteries on short- and long-term outcomes: a propensity score matching in

accordance with current recommendations. J Thorac Cardiovasc Surg. 2014;148:2699-705.

9. Benedetto U, Codispoti M. Age cutoff for the loss of survival benefit from use of radial artery in coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2013;146:1078-84.
10. Suzuki T, Asai T, Nota H, Kinoshita T, Fujino S. Impact Of Total Arterial Reconstruction on Long Term Mortality and Morbidity: Off-Pump Total Arterial Reconstruction Versus Non-Total Arterial Reconstruction. Ann Thorac Surg. 2015;100:2244-9.
11. Kinoshita T, Asai T, Suzuki T, Kambara A, Matsubayashi K. Off-pump bilateral versus single skeletonized internal thoracic artery grafting in high-risk patients. Circulation. 2011 Sep 13;124(11 Suppl):S130-4
12. Navia D, Vrancic M, Piccinini F, Camporrotondo M, Thierer J, Gil C et al.Is the second internal thoracic artery better than the radial artery in total arterial off-pump coronary artery bypass grafting? A propensity score-matched follow-up study. J Thorac Cardiovasc Surg. 2014;147:632-8
13. van Dijk D, Nierich AP, Jansen EW, Nathoe HM, Suyker WLL, Diephuis JC et al. Early outcome after off-pump versus on-pump coronary artery bypass surgery: results from a randomized study. Circulation. 2001;104:1761–1766.
14. Angelini GD, Taylor FC, Reeves BC, Ascione R. Early and midterm outcome after off-pump and on-pump surgery in beating heart against Cardioplegic Arrest Studies (BHACAS 1 and 2): a pooled analysis of two randomized controlled trials. Lancet. 2002;359:1194 –1199.

15. Nathoe HM, van Dijk D, Jansen EW, Suyker WIL, Diephuis JC, van Boven WJ et al. A comparison of off-pump and on-pump coronary bypass surgery in low-risk patients. N Eng J Med. 2003;348:394–402.
16. Khan NE, De Souza A, Mister R, Flather M, Clague J, Davies S, Collins P, Wang D, Sigwart U, Pepper J. A randomized comparison of off-pump and on-pump multivessel coronary-artery bypass surgery. N Eng J Med. 2004;350:21–28.
17. Puskas JD, Williams WH, Duke PG, Staples JR, Glas KE, Marshall JJ et al. Off-pump coronary artery bypass grafting provides complete revascularization with reduced myocardial injury, transfusion requirements, and length of stay: a prospective randomized comparison of 200 unselected patients undergoing off-pump versus conventional coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2003;125:797– 808.
18. Le´gare´ JF, Buth KJ, King S, Wood J, Sullivan JA, Friesen CH et al. Coronary bypass surgery performed off pump does not result in lower in-hospital morbidity than coronary artery bypass grafting performed on pump. Circulation. 2004;109:887– 892.
19. Rubin, D.B. (1987) *Multiple Imputation for Nonresponse in Surveys*. J. Wiley & Sons, New York.
20. McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med. 2013;32:3388-414
21. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates Publishers; 1988.
22. Lauer MS, Blackstone EH, JYoung JB, Topol EJ. Cause of death in clinical research: time for a reassessment? J Am Coll Cardiol 1999;34:618–20

23. The Society of Thoracic Surgeons. Fall 2009 report: adult cardiac database executive summary.http://www.sts.org/sections/stsnationaldatabase/publications/executive/article.html. Accessed January 24, 2009.
24. Kobayashi J, Tashiro T, Ochi M, Yaku H, Watanabe G, Satoh T et al; Japanese Off-Pump Coronary Revascularization Investigation (JOCRI) Study Group. Early outcome of a randomized comparison of off-pump and on-pump multiple arterial coronary revascularization. Circulation. 2005 Aug 30;112(9 Suppl):I338-43.
25. Taggart DP, Altman DG, Gray AM, Lees B, Nugara F, Yu LM et al. Effects of on-pump and off-pump surgery in the Arterial Revascularization Trial. Eur J Cardiothorac Surg. 2015;47:1059-65.
26. Omer S, Cornwell LD, Rosengart TK, Kelly RF, Ward HB, Holman WL et al. Completeness of coronary revascularization and survival: Impact of age and off-pump surgery. J Thorac Cardiovasc Surg. 2014;148:1307-15
27. Puskas JD, Williams WH, O'Donnell R, Patterson RE, Sigman SR, Smith AS et ak.Off-pump and on-pump coronary artery bypass grafting are associated with similar graft patency, myocardial ischemia, and freedom from reintervention: long-term follow-up of a randomized trial. Ann Thorac Surg. 2011;91:1836-42

Table 1. Pre-treatment variables in the unweighted population

	SA-ONCAB		MA-ONCAB		SA-OPCAB		MA-OPCAB		Max ASDM
	N=5194		N=1208		N= 4412		N=1818		
	n	%	n	%	n	%	n	%	
Age (years, sd)	68±8		57±8		69±9		61±9		121%
Female	935	18	109	9	838	19	218	12	26%
CCS III-IV	1610	31	290	24	1324	30	382	21	21%
NYHA III-IV	2701	52	580	48	1985	45	782	43	18%
MI within 30days	987	19	145	12	971	22	345	19	26%
PCI	208	4	36	3	265	6	109	6	15%
DM orally treated	571	11	72	6	485	11	164	9	18%
DM on insulin	364	7	60	5	353	8	109	6	12%
Current smoking	623	12	217	18	529	12	273	15	18%
Creatinine≥200mmol/l	156	3	12	1	132	3	18	1	16%
COPD	416	8	36	3	353	8	91	5	2%
CVA	208	4	36	3	176	4	36	2	11%
PVD	571	11	72	6	485	11	127	7	15%
Atrial fibrillation	208	4	24	2	176	4	36	2	8%
3-vessel disease	4155	80	870	72	3044	69	1218	67	3%
Left main disease	1299	25	242	20	1279	29	509	28	21%
LVEF between 30-49%	1195	23	205	17	1015	23	291	16	17%
LVEF ≤30%	312	6	36	3	221	5	18	1	21%
Cardiogenic shock	52	1	0	0	0	0	0	0	11%
Preoperative IABP	104	2	0	0	44	1	0	0	12%
Non-elective admission	2545	49	507	42	2162	49	745	41	16%
Emergent/salvage	52	1	0	0	44	1	18	1	1%
BMI	28±5		28±4		28±4		28±4		19%
Year of surgery	2004±6		2002±4		2007±4		2006±4		92%
Logistic Euroscore	4.3±4.8		2.1±2.2		4.5±4.8		2.5±2.8		

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; NYHA: New York Heart Associatio; CCS: Canadian Cardiovascular Society; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; BMI: body mass index; ASMD: absolute standardized mean difference

Table 2. Pre-treatment variables in the PS-weighted population

	SA-ONCAB		MA-ONCAB		SA-OPCAB		MA-OPCAB		Max ASDM
	ESS=3972		ESS=388		ESS=2567		ESS=739		
	n	%	n	%	n	%	n	%	
Age (years, sd)	66±10		65±10		66±9		65±9		14%
Female	675	17	58	15	410	16	118	16	6%
NYHA III-IV	1906	48	186	48	1206	47	339	46	4%
CCS III-IV	1151	29	116	30	744	29	199	27	8%
MI within 30 days	794	20	69	18	487	19	147	20	4%
PCI	198	5	19	5	128	5	44	6	4%
DM orally treated	397	10	38	10	282	11	73	10	2%
DM on insulin	278	7	19	5	179	7	44	6	10%
Current smoking	556	14	46	12	333	13	88	12	5%
Creatinine≥200mmol/l	79	2	3	1	51	2	7	1	10%
COPD	278	7	27	7	179	7	44	6	5%
CVA	158	4	15	4	102	4	14	2	10%
PVD	397	10	31	8	256	10	59	8	7%
Atrial fibrillation	119	3	15	4	77	3	22	3	6%
3-vessel disease	2939	74	279	72	1848	72	524	71	8%
Left main disease	1032	26	100	26	693	27	192	26	2%
LVEF between 30-49%	873	22	89	23	539	21	147	20	8%
LVEF ≤30%	198	5	23	6	102	4	22	3	16%
Cardiogenic shock	0	0	0	0	0	0	0	0	7%
Preoperative IABP	39	1	0	0	25	1	7	1	9%
Non-elective admission	1866	47	182	47	1232	48	332	45	6%
Emergent/salvage	39	1	3	1	25	1	7	1	6%
BMI	28±4		28±4		28±4		28±4		8%
Year of surgery	2005±4		2005±6		2006±6		2005±8		13%

Logistic Euroscore	3.9±3.8		3.7±5.9		3.9±3.6		3.6±4.1			

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; **EES: effective sample size;** NYHA: New York Heart Association; CCS: Canadian Cardiovascular Society**;** MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; BMI: body mass index; ASMD: absolute standardized mean difference

Table 3. Intraoperative data

		SA-ONCAB N=5194		MA-ONCAB N=1208		SA-OPCAB N=4412		MA-OPCAB N=1818		$\chi 2$ P-value
		N	%	n	%	n	%	n	%	
MA configuration	BITA	-	-	420	34.8	-	-	335	18.4	<0.0001
	RA			617	51.1			1384	76.2	
	BITA+RA			171	14.1			99	5.4	
Total arterial Revascularization	No			708	58.6			1031	56.7	0.31
	Yes			500	41.4			787	43.3	
Number of grafts	1	1	0.0	1	0.1	0	0.0	0	0.0	<0.0001
	2	1004	19.3	330	27.3	1662	37.7	645	35.5	
	3	3020	58.1	609	50.4	2383	54.0	913	50.2	
	4	1106	21.3	249	20.6	357	8.1	252	13.9	
	5	62	1.2	19	1.6	9	0.2	8	0.4	
	6	1	0.0	0	0.0	1	0.0	0	0.0	
Mean grafts/pt		3.04±0.67		2.96±0.74		2.71± 0.62		2.79±0.68		<0.0001
LAD territory grafted	No	89	1.7	22	1.8	89	2.0	43	2.4	0.3
	Yes	5105	98.3	1186	98.2	4323	98.0	1775	97.6	
RCA territory grafted	No	1265	24.4	316	26.2	1406	31.9	609	33.5	<0.0001
	Yes	3929	75.6	892	73.8	3006	68.1	1209	66.5	
CX territory grafted	No	655	12.6	208	17.2	1031	23.4	323	17.8	<0.0001
	Yes	4539	87.4	1000	82.8	3381	76.6	1495	82.2	
Diagonal branch grafted	No	3887	74.8	915	75.7	3607	81.8	1428	78.5	<0.0001

	Yes	1307	25.2	293	24.3	805	18.2	390	21.5	
Sequential anastomosis	No	4956	95.4	1130	93.5	4097	92.9	1694	93.2	<0.0001
	Yes	238	4.6	78	6.5	315	7.1	124	6.8	

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; BITA: bilateral internal thoracic arteries; RA: Radial artery; LAD: left anterior descending artery; RCA: right coronary artery; CX: circumflex artery.

Table 4. Incidence of postoperative outcomes

		SA-ONCAB N=5194		**MA-ONCAB N=1208**		**SA-OPCAB N=4412**		**MA-OPCAB N=1818**		**$\chi 2$ P-value**
		N	%	n	%	n	%	n	%	
Mortality within 30 days	No	5125	98.7	1201	99.4	4344	98.5	1810	99.6	0.0005
	Yes	69	1.3	7	0.6	68	1.5	8	0.4	
Postoperative CVA	No	5112	98.4	1197	99.1	4348	98.5	1808	99.4	0.005
	Yes	82	1.6	11	0.9	64	1.5	10	0.6	
Postoperative IABP	No	5023	96.7	1188	98.3	4318	97.9	1796	98.8	<0.0001
	Yes	171	3.3	20	1.7	94	2.1	22	1.2	
Postoperative RRT	No	5075	97.7	1192	98.7	4299	97.4	1799	99.0	0.003
	Yes	119	2.3	16	1.3	113	2.6	19	1.0	
Sternal wound reconstruction	No	5157	99.3	1204	99.7	4376	99.2	1808	99.4	0.3
	Yes	37	0.7	4	0.3	36	0.8	10	0.6	
Re-exploration	No	5021	96.7	1164	96.4	4312	97.7	1786	98.2	0.0001
	Yes	173	3.3	44	3.6	100	2.3	32	1.8	
IR	No	4888	94.1	1145	94.8	3898	88.3	1659	91.3	<0.0001
	Yes	306	5.9	63	5.2	514	11.7	159	8.7	

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; CVA: cerebrovascular accident; IABP: intra-aortic balloon pump; RRT: renal replacement therapy; IR: incomplete revascularization

Table 5. PS-weighted estimates (SA-ONCAB as a reference group; Bold: P<0.05)

	Treatment group	Crude ES[95%CI]	crude P value	PS-weighted ES[95%CI]	PS-weighted P value
Mortality within 30 days	MA-ONCAB	0.43[0.20-0.94]	0.03	0.96[0.28- 3.22]	0.95
	SA-OPCAB	1.16[0.83-1.62]	0.38	0.96[0.67-1.39]	0.86
	MA-OPCAB	0.33[0.16-0.69]	0.03	0.44[0.18-1.08]	0.07
Postoperative CVA	MA-ONCAB	0.57[0.30-1.08]	0.08	1.84[0.72-4.70]	0.20
	SA-OPCAB	0.92[0.66-1.28]	0.60	1.08[0.72-1.63]	0.70
	MA-OPCAB	0.35[0.18-0.67]	0.001	0.90[0.38-2.11]	0.81
Postoperative IABP	MA-ONCAB	0.49[0.31-0.79]	0.003	1.67[0.88-3.15]	0.11
	SA-OPCAB	0.64[0.50-0.83]	<0.0001	0.69[0.51-0.92]	0.01
	MA-OPCAB	0.36[0.23-0.56]	<0.0001	0.70[0.41-1.20]	0.20
Postoperative RRT	MA-ONCAB	0.57[0.34-0.97]	0.03	1.23[0.55-2.76]	0.61
	SA-OPCAB	1.12[0.86-1.46]	0.39	1.15[0.86-1.54]	0.34
	MA-OPCAB	0.45[0.28-0.73]	0.001	0.82[0.41-1.63]	0.57
Sternal wound reconstruction	MA-ONCAB	0.46[0.16-1.30]	0.14	2.33[0.64-8.39]	0.20
	SA-OPCAB	1.15[0.72-1.82]	0.46	1.10[0.50-2.40]	0.59
	MA-OPCAB	0.77[0.38-1.55]	0.56	0.87[0.54-1.41]	0.81
Re-exploration	MA-ONCAB	1.10[0.78-1.54]	0.59	1.18[0.68-2.03]	0.55
	SA-OPCAB	0.67[0.52-0.86]	<0.0001	0.66[0.51-0.87]	0.002
	MA-OPCAB	0.52[0.36-0.76]	<0.0001	0.78[0.49-1.24]	0.28
IR	MA-ONCAB	0.88[0.66-1.15]	0.36	1.002[0.61-1.65]	0.99
	SA-OPCAB	2.11[1.82-2.44]	<0.0001	2.39[2.01-2.86]	<0.0001
	MA-OPCAB	1.53[1.25-1.86]	<0.0001	2.04[1.54-2.68]	<0.0001

Late mortality (beyond 30 days)	MA-ONCAB	0.36[0.31-0.42]	<0.0001	0.81[0.649-0.99]	0.04
	SA-OPCAB	1.14[1.05-1.24]	0.001	1.07[0.96-1.19]	0.20
	MA-OPCAB	0.56[0.49-0.64]	<0.0001	0.81[0.69-0.98]	0.03

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; CVA: cerebrovascular accident; IABP: intra-aortic balloon pump; RRT: renal replacement therapy; IR: incomplete revascularization.

Supplementary Table 1. Absolute standardized mean difference (ASMD) for each variable among groups comparison in the unweighted population

Variable	Group 1	Group 2	ASMD		Group 1	Group 2	ASMD
Age	SAONCAB	MAONCAB	110%		MAONCAB	MAOPCAB	42%
Female	SAONCAB	MAONCAB	25%		MAONCAB	MAOPCAB	7%
NYHA III-IV	SAONCAB	MAONCAB	7%		MAONCAB	MAOPCAB	11%
CCS III-IV	SAONCAB	MAONCAB	14%		MAONCAB	MAOPCAB	7%
MI within 30 days	SAONCAB	MAONCAB	18%		MAONCAB	MAOPCAB	18%
PCI	SAONCAB	MAONCAB	7%		MAONCAB	MAOPCAB	15%
DM orally treated	SAONCAB	MAONCAB	16%		MAONCAB	MAOPCAB	11%
DM on insulin	SAONCAB	MAONCAB	9%		MAONCAB	MAOPCAB	2%
Current smoking	SAONCAB	MAONCAB	17%		MAONCAB	MAOPCAB	8%
Creatinine≥200mmol/l	SAONCAB	MAONCAB	14%		MAONCAB	MAOPCAB	0%
COPD	SAONCAB	MAONCAB	18%		MAONCAB	MAOPCAB	5%
CVA	SAONCAB	MAONCAB	7%		MAONCAB	MAOPCAB	2%
PVD	SAONCAB	MAONCAB	14%		MAONCAB	MAOPCAB	2%
Atrial fibrillation	SAONCAB	MAONCAB	8%		MAONCAB	MAOPCAB	0%
3-vessel disease	SAONCAB	MAONCAB	19%		MAONCAB	MAOPCAB	11%
Left main disease	SAONCAB	MAONCAB	12%		MAONCAB	MAOPCAB	18%
LVEF between 30-49%	SAONCAB	MAONCAB	15%		MAONCAB	MAOPCAB	2%
LVEF ≤30%	SAONCAB	MAONCAB	15%		MAONCAB	MAOPCAB	6%
Cardiogenic shock	SAONCAB	MAONCAB	11%		MAONCAB	MAOPCAB	1%
Preoperative IABP	SAONCAB	MAONCAB	12%		MAONCAB	MAOPCAB	2%
Non-elective admission	SAONCAB	MAONCAB	15%		MAONCAB	MAOPCAB	1%
Emergent/salvage	SAONCAB	MAONCAB	10%		MAONCAB	MAOPCAB	1%
BMI	SAONCAB	MAONCAB	12%		MAONCAB	MAOPCAB	7%

Year of surgery	SAONCAB	MAONCAB	44%		MAONCAB	MAOPCAB	77%
Age	SAONCAB	MAOPCAB	68%		MAONCAB	SAOPCAB	121%
Female	SAONCAB	MAOPCAB	18%		MAONCAB	SAOPCAB	26%
NYHA III-IV	SAONCAB	MAOPCAB	18%		MAONCAB	SAOPCAB	7%
CCS III-IV	SAONCAB	MAOPCAB	21%		MAONCAB	SAOPCAB	12%
MI within 30 days	SAONCAB	MAOPCAB	0%		MAONCAB	SAOPCAB	26%
PCI	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	15%
DM orally treated	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	18%
DM on insulin	SAONCAB	MAOPCAB	7%		MAONCAB	SAOPCAB	12%
Current smoking	SAONCAB	MAOPCAB	9%		MAONCAB	SAOPCAB	18%
Creatinine≥200mmol/l	SAONCAB	MAOPCAB	14%		MAONCAB	SAOPCAB	16%
COPD	SAONCAB	MAOPCAB	13%		MAONCAB	SAOPCAB	20%
CVA	SAONCAB	MAOPCAB	10%		MAONCAB	SAOPCAB	8%
PVD	SAONCAB	MAOPCAB	12%		MAONCAB	SAOPCAB	15%
Atrial fibrillation	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	8%
3-vessel disease	SAONCAB	MAOPCAB	30%		MAONCAB	SAOPCAB	7%
Left main disease	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	21%
LVEF between 30-49%	SAONCAB	MAOPCAB	17%		MAONCAB	SAOPCAB	15%
LVEF ≤30%	SAONCAB	MAOPCAB	21%		MAONCAB	SAOPCAB	11%
Cardiogenic shock	SAONCAB	MAOPCAB	10%		MAONCAB	SAOPCAB	4%
Preoperative IABP	SAONCAB	MAOPCAB	10%		MAONCAB	SAOPCAB	11%
Non-elective admission	SAONCAB	MAOPCAB	16%		MAONCAB	SAOPCAB	13%
Emergent/salvage	SAONCAB	MAOPCAB	9%		MAONCAB	SAOPCAB	6%
BMI	SAONCAB	MAOPCAB	19%		MAONCAB	SAOPCAB	2%
Year of surgery	SAONCAB	MAOPCAB	33%		MAONCAB	SAOPCAB	92%
Age	SAONCAB	SAOPCAB	12%		MAOPCAB	SAOPCAB	79%
Female	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	18%
NYHA III-IV	SAONCAB	SAOPCAB	14%		MAOPCAB	SAOPCAB	4%

CCS III-IV	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	20%
MI within 30 days	SAONCAB	SAOPCAB	8%		MAOPCAB	SAOPCAB	8%
PCI	SAONCAB	SAOPCAB	8%		MAOPCAB	SAOPCAB	0%
DM orally treated	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	7%
DM on insulin	SAONCAB	SAOPCAB	3%		MAOPCAB	SAOPCAB	10%
Current smoking	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	10%
Creatinine≥200mmol/l	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	16%
COPD	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	15%
CVA	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	11%
PVD	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	13%
Atrial fibrillation	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	8%
3-vessel disease	SAONCAB	SAOPCAB	26%		MAOPCAB	SAOPCAB	4%
Left main disease	SAONCAB	SAOPCAB	9%		MAOPCAB	SAOPCAB	3%
LVEF between 30-49%	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	17%
LVEF ≤30%	SAONCAB	SAOPCAB	5%		MAOPCAB	SAOPCAB	16%
Cardiogenic shock	SAONCAB	SAOPCAB	7%		MAOPCAB	SAOPCAB	3%
Preoperative IABP	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	9%
Non-elective admission	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	14%
Emergent/salvage	SAONCAB	SAOPCAB	4%		MAOPCAB	SAOPCAB	4%
BMI	SAONCAB	SAOPCAB	10%		MAOPCAB	SAOPCAB	9%
Year of surgery	SAONCAB	SAOPCAB	48%		MAOPCAB	SAOPCAB	15%

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; NYHA: New York Heart Association: CCS: Scandinavian cardiovascular Society; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; BMI: body mass index; ASMD: absolute standardized mean difference

Supplementary Figure 2. Absolute standardized mean difference (ASMD) for each variable among groups comparison after inverse Propensity score weighting

Variable	Group 1	Group 2	ASMD		Group 1	Group 2	ASMD
Age	SAONCAB	MAONCAB	11%		MAONCAB	MAOPCAB	1%
Female	SAONCAB	MAONCAB	6%		MAONCAB	MAOPCAB	2%
NYHA III-IV	SAONCAB	MAONCAB	0%		MAONCAB	MAOPCAB	4%
CCS III-IV	SAONCAB	MAONCAB	4%		MAONCAB	MAOPCAB	8%
MI within 30 days	SAONCAB	MAONCAB	4%		MAONCAB	MAOPCAB	4%
PCI	SAONCAB	MAONCAB	0%		MAONCAB	MAOPCAB	4%
DM orally treated	SAONCAB	MAONCAB	1%		MAONCAB	MAOPCAB	2%
DM on insulin	SAONCAB	MAONCAB	10%		MAONCAB	MAOPCAB	6%
Current smoking	SAONCAB	MAONCAB	5%		MAONCAB	MAOPCAB	0%
Creatinine≥200mmol/l	SAONCAB	MAONCAB	10%		MAONCAB	MAOPCAB	4%
COPD	SAONCAB	MAONCAB	0%		MAONCAB	MAOPCAB	5%
CVA	SAONCAB	MAONCAB	2%		MAONCAB	MAOPCAB	10%
PVD	SAONCAB	MAONCAB	5%		MAONCAB	MAOPCAB	1%
Atrial fibrillation	SAONCAB	MAONCAB	4%		MAONCAB	MAOPCAB	4%
3-vessel disease	SAONCAB	MAONCAB	6%		MAONCAB	MAOPCAB	2%
Left main disease	SAONCAB	MAONCAB	0%		MAONCAB	MAOPCAB	1%
LVEF between 30-49%	SAONCAB	MAONCAB	3%		MAONCAB	MAOPCAB	8%
LVEF ≤30%	SAONCAB	MAONCAB	7%		MAONCAB	MAOPCAB	16%
Cardiogenic shock	SAONCAB	MAONCAB	7%		MAONCAB	MAOPCAB	2%
Preoperative IABP	SAONCAB	MAONCAB	9%		MAONCAB	MAOPCAB	4%
Non-elective admission	SAONCAB	MAONCAB	1%		MAONCAB	MAOPCAB	4%

Emergent/salvage	SAONCAB	MAONCAB	5%		MAONCAB	MAOPCAB	1%
BMI	SAONCAB	MAONCAB	5%		MAONCAB	MAOPCAB	3%
Year of surgery	SAONCAB	MAONCAB	5%		MAONCAB	MAOPCAB	13%
Age	SAONCAB	MAOPCAB	10%		MAONCAB	SAOPCAB	14%
Female	SAONCAB	MAOPCAB	4%		MAONCAB	SAOPCAB	4%
NYHA III-IV	SAONCAB	MAOPCAB	4%		MAONCAB	SAOPCAB	2%
CCS III-IV	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	3%
MI within 30 days	SAONCAB	MAOPCAB	0%		MAONCAB	SAOPCAB	3%
PCI	SAONCAB	MAOPCAB	4%		MAONCAB	SAOPCAB	0%
DM orally treated	SAONCAB	MAOPCAB	0%		MAONCAB	SAOPCAB	2%
DM on insulin	SAONCAB	MAOPCAB	4%		MAONCAB	SAOPCAB	9%
Current smoking	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	3%
Creatinine≥200mmol/l	SAONCAB	MAOPCAB	6%		MAONCAB	SAOPCAB	9%
COPD	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	1%
CVA	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	1%
PVD	SAONCAB	MAOPCAB	7%		MAONCAB	SAOPCAB	5%
Atrial fibrillation	SAONCAB	MAOPCAB	0%		MAONCAB	SAOPCAB	6%
3-vessel disease	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	0%
Left main disease	SAONCAB	MAOPCAB	1%		MAONCAB	SAOPCAB	1%
LVEF between 30-49%	SAONCAB	MAOPCAB	6%		MAONCAB	SAOPCAB	4%
LVEF ≤30%	SAONCAB	MAOPCAB	9%		MAONCAB	SAOPCAB	8%
Cardiogenic shock	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	4%
Preoperative IABP	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	9%
Non-elective admission	SAONCAB	MAOPCAB	5%		MAONCAB	SAOPCAB	1%
Emergent/salvage	SAONCAB	MAOPCAB	6%		MAONCAB	SAOPCAB	2%
BMI	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	5%

Year of surgery	SAONCAB	MAOPCAB	8%		MAONCAB	SAOPCAB	13%
Age	SAONCAB	SAOPCAB	3%		MAOPCAB	SAOPCAB	13%
Female	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	2%
NYHA III-IV	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	2%
CCS III-IV	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	6%
MI within 30 days	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	1%
PCI	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	4%
DM orally treated	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	0%
DM on insulin	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	4%
Current smoking	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	3%
Creatinine≥200mmol/l	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	6%
COPD	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	4%
CVA	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	9%
PVD	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	6%
Atrial fibrillation	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	1%
3-vessel disease	SAONCAB	SAOPCAB	6%		MAOPCAB	SAOPCAB	2%
Left main disease	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	2%
LVEF between 30-49%	SAONCAB	SAOPCAB	1%		MAOPCAB	SAOPCAB	5%
LVEF ≤30%	SAONCAB	SAOPCAB	2%		MAOPCAB	SAOPCAB	8%
Cardiogenic shock	SAONCAB	SAOPCAB	3%		MAOPCAB	SAOPCAB	2%
Preoperative IABP	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	5%
Non-elective admission	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	6%
Emergent/salvage	SAONCAB	SAOPCAB	3%		MAOPCAB	SAOPCAB	3%
BMI	SAONCAB	SAOPCAB	0%		MAOPCAB	SAOPCAB	8%
Year of surgery	SAONCAB	SAOPCAB	8%		MAOPCAB	SAOPCAB	1%

SA: single Artery; MA: multiple arteries; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass; NYHA: New York Heart Association: CCS: Scandinavian cardiovascular Society; MI: myocardial infarction; PCI: percutaneous coronary intervention; DM: diabetes mellitus; COPD: chronic obstructive pulmonary

disease; CVA: cerebrovascular accident; PVD: peripheral vascular disease; LVEF: left ventricular ejection fraction; IABP: intra-aortic balloon pump; BMI: body mass index; ASMD: absolute standardized mean difference

Figure Legends.

Figure 1. Number of multiple arterial (MA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery during the study period.

Figure 2. Survival rate in the unweighted (left) and propensity score weighted (right) multiple arterial (MA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery groups (± standard errors at 5,10 and 15 years are reported for each propensity score weighted group).

Supplementary Figure 1. Change in maximum absolute standardized mean differences before and after propensity score weighting.

Supplementary Figure 2. Survival rate in the unweighted multiple arterial (MA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery groups according to completeness of revascularization.

Supplementary Figure 3. Survival rate in the unweighted multiple arterial (MA) plus saphenous vein (SV), total arterial (TA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery groups.

Supplementary Figure 4. Survival rate in the unweighted multiple arterial (MA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery groups across eras of surgery.

Central picture: Survival rate in the propensity score weighted multiple arterial (MA) and single arterial (SA) off-pump coronary artery bypass (OPCAB) and on pump coronary artery bypass (ONCAB) surgery groups. (±standard errors at 5,10 and 15 years are reported for each propensity score weighted group).

Video 1. Use of the Radial Artery during off-pump coronary artery bypass